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Outcomes of office-based, open food challenges in the management of food allergy

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Abstract

This letter reports the largest series of open oral food challenges in the literature to date. It describes the feasibility and utility of oral food challenge, further justifying its use in the everyday practice of allergy.

Keywords

Food Allergy; Oral Food Challenge; Outpatient; Skin Test; Peanut

To the Editor

Given the increasing use of diagnostic testing and an apparent increase in food allergy prevalence¹, it is vital that allergists correctly identify patients with clinical reactivity to foods as opposed to sensitization only. With the use of a detailed medical history, skin testing and food-specific serum IgE levels, physicians can often predict the likelihood of an allergic reaction if a particular food is ingested, although in many instances the oral food challenge (OFC) is required to definitively prove tolerance.² The double-blind, placebo-controlled OFC is the accepted gold standard for this, but such challenges can be expensive, time-consuming, and, for most practicing allergists, are often not feasible in the everyday office setting. While the open OFC is an accepted alternative, few studies have examined the test's feasibility, efficacy and safety.^{3–5}

We report results from a retrospective chart review of all open OFCs performed at the Jaffe Food Allergy Institute, a university-based, outpatient practice, between August 2008 and

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May 2010. All patients were referred for open OFC based on allergists' clinical impression in conjunction with family interests (i.e. likelihood of reaction was discussed with families and an OFC was offered unless it was felt by the allergist to be too high risk). Patients were referred by 9 different allergists. No specific cut-off serum IgE value or skin test size precluded challenge; however, patients were typically not referred if the likelihood of a positive reaction was thought to be greater than 50%.² Serum IgE (sIgE) levels (ImmunoCAP; Phadia, Uppsala, Sweden) and/or skin prick testing (SPT) using standardized extracts (Greer[®] Laboratories, NC, USA) were performed within 6 months of the OFC on all patients. The OFCs were performed in the outpatient setting by a trained nurse or physician (while the supervising physician was on site at all times) per guidelines established by the current Working Group on Food Challenges report, with most challenges using doubling doses every 15 minutes until an age appropriate serving size was administered.⁶ For subjective symptoms, challenges were temporarily paused and then continued following resolution of symptoms if the supervising physician deemed it safe to proceed. All treatment decisions were based on the supervising clinician's judgment. All patients were monitored for at least 2 hours post-challenge and instructed to contact the clinic for any delayed reactions.

We performed a total of 701 open OFCs in 521 different patients. The majority of the patients were male (62.6%) and ages ranged from 8 months to 21.8 years (median = 5.67 years). Overall, 132 (18.8%) of the challenges elicited a reaction. There were no differences in age or gender between the group that passed the OFCs and the group that failed. Breakdown of challenge results by food are shown in Table 1.

Patients who passed the OFC without adverse symptoms had significantly smaller SPT wheal size (median = 3.00 mm [0 – 9 mm] vs 4.00 mm [0 – 12 mm], $p = 0.0001$) and significantly lower sIgE levels to the challenged foods (median = 0.63 kU_A/L [0.0 – >100] vs 1.06 kU_A/L [0.0 – 68.2], $p = 0.027$) as compared to the group that reacted during the OFC (Table 2). Patients who had an identifiable history of anaphylaxis to the challenged food were more likely to react during the OFC (5/13, 38.5%) than those who did not have a history of anaphylaxis (127/684, 18.6%), but this difference did not reach statistical significance ($p = 0.08$). In addition, patients who had never actually ingested the challenged food, but were avoiding it due to evidence of sensitization, were less likely to react during the OFC (46/328, 14.0%) as compared to those patients who had previously ingested the challenged food and reacted (86/361, 23.8%), $p = 0.0013$.

The majority of reactions, 56.8%, were cutaneous. All but 16 reactions (87.9%) were treated with antihistamine alone. Twelve reactions were treated with epinephrine (including one which required 2 doses of epinephrine), 7 with prednisolone, and 2 with albuterol (Table 3). All but one reaction was managed in the office setting; one patient was transferred to the emergency room for monitoring and intravenous fluids due to persistent vomiting following a challenge to peanut.

With growing numbers of patients presenting to allergists with laboratory findings of food sensitization and low-likelihood of reaction, it is imperative that the allergist be able to give patients and parents a definitive answer regarding their allergic status. Clinical history, SPT, and sIgE levels can only provide data to suggest the likelihood of reaction. While a double-blind challenge is the optimal method for defining clinical reactivity, it may not be feasible in a busy, outpatient practice. An open challenge requires less time and resources, and provides the parent/patient with objective evidence of tolerance or reactivity. In this largest study of open OFCs to date, we show that the procedure can be done in a high volume practice, with approximately 35 challenges being performed per month. While no specific inclusion or exclusion cut-off criteria were utilized for OFC referrals, we believe that this

cohort is highly reflective of a population encountered in a typical allergy practice, especially given that the reported cohort represents patients referred by 9 different physicians. Given the median specific IgE levels and the skin test results, the majority of these patients were at relatively “low-risk” for reaction, however, it is this exact population for which the risk-to-benefit ratio is optimal for performing an OFC. A previous report of open OFC by Perry et al. in a higher risk population (i.e. individuals with higher median specific IgE levels) demonstrated an OFC reaction rate of 43%, a rate which is higher than may be desirable for a busy office practice.³ In fact, by ruling out clinical reactivity in over 80% of our patients, we were able to add foods back into the diets of the majority of patients. Utilizing such challenges avoids the need to have these “low-risk” patients ingest and potentially experience allergic reactions to the food at home. For example, while SPTs overall showed strong negative predictive values, there were 23 patients with negative skin tests who reacted to the food, 3 of whom had significant systemic reactions. In addition, 34 patients with undetectable food-specific IgE had reactions during OFC and 10 patients who reacted had both negative SPT and sIgE results. Some of these reactions likely represent false-positive OFCs (e.g. persistent subjective symptoms in anxious patients) or non-IgE-mediated reactions, but had they occurred after introduction of the food at home, they may have put the patient at risk and the family under unnecessary stress. For highly anxious patients or for those experiencing equivocal symptoms, it may be advisable to perform blinded OFCs in order to reduce the likelihood of a false-positive OFC. Finally, we have shown that in this population, the open OFC is safe, provided it is carried out in an allergist’s office. Only 1.7% of challenges required treatment with epinephrine, a rate that is equivalent to or lower than most published studies on systemic reactions to subcutaneous immunotherapy.⁷

In conclusion, open OFC’s are safe and effective for establishing tolerance in patients with suspected food allergy.

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Table 1

Results of all challenges, broken down by specific food and organ system of reaction.

Food	Number (% of all challenges)	Number Positive (%)	Reaction Organ Involvement				
			Skin	Oral/Nasal symptoms	Lower Respiratory	Gastro-intestinal	>1 system
Peanut	124 (17.7%)	26 (21.0%)	16	1	1	6	2
Tree Nuts	121 (17.0%)	22 (18.2%)	7	13	0	1	1
Egg	112 (16.0%)	15 (13.4%)	8	2	1	1	3
Milk	55 (7.8%)	22 (40.0%)	14	6	0	2	0
Soy	54 (7.7%)	10 (18.5%)	7	2	1	0	0
Fish*	49 (6.9%)	6 (12.2%)	4	2	0	0	0
Sesame	44 (6.3%)	7 (15.9%)	4	1	0	1	1
Shellfish [†]	29 (4.1%)	3 (10.3%)	1	2	0	0	0
Wheat	28 (4.0%)	6 (21.4%)	4	0	0	0	2
Other	85 (12.1%)	15 (17.6%)	10	2	0	2	1
All Foods	701	132 (18.8%)	75	31	3	13	10

* Fish causing reactions include codfish, halibut, tilapia, and tuna (3)

[†] All shellfish reactions to shrimp

Table 2

Skin test results and serum IgE levels for the most commonly challenged foods (i.e. foods with 50 Challenges or more)

Food	Skin Test (mm)			Serum IgE (kU _A /L)			p-value
	Positive Challenge	Negative Challenge	p-value	Positive Challenge	Negative Challenge	p-value	
Peanut	4.00 (0 – 12)	2.00 (0 – 8)	0.0009	0.36 (0.0 – 6.0)	0.18 (0.0 – 6.7)	0.734	0.734
Tree Nuts	4.00 (0 – 7)	1.00 (0 – 7)	0.0012	0.44 (0.0 – 9.5)	0.00 (0.0 – 13.6)	0.387	0.387
Egg	4.00 (0 – 10)	3.00 (0 – 8)	0.0419	1.30 (0.0 – 2.7)	0.59 (0.0 – 4.9)	0.229	0.229
Milk	5.00 (0 – 8)	3.00 (0 – 8)	0.0048	0.97 (0.0 – 7.1)	0.58 (0.0 – 25.7)	0.308	0.308
Soy	5.00 (0 – 8)	3.00 (0 – 9)	0.0899	4.26 (0.74 – 25.2)	3.41 (0.0 – 29.3)	0.659	0.659
All Foods	4.00 (0 – 12)	3.00 (0 – 9)	<0.0001	1.06 (0.0 – >100)	0.63 (0.0 – 68.2)	0.027	0.027

* skin test results and serum IgE levels displayed as medians (ranges)

Table 3

Patients requiring epinephrine

Age	Food	Clinical History	SPT	sIgE	Reaction	Dose Causing Reaction
9.2 years	Beef	Urticaria	7 mm	3.60	A, U, V	3 oz hamburger (~ 20 grams protein)
12.6 years	Egg	Never ingested	4 mm	2.28	C, W, U	1 gram protein
4.2 years	Egg	Eczema flare	10 mm	1.91	V, U	1/10 egg (~ 0.75 grams protein)
5.5 years	Peanut	Never Ingested	2 mm	<0.35	V*	2 tablespoons peanut butter (~ 8 grams protein)
5.75 years	Peanut	Never Ingested	0 mm	3.71	C, W, D	1 teaspoon peanut butter (~ 1.3 grams protein)
4.8 years	Peanut	Never Ingested	5 mm	<0.35	S, C, U	5 grams protein
5.1 years	Peanut	No known reactions	4 mm	1.65	S, C, U, V	5/8 tablespoon peanut butter (~ 2.5 grams protein)
14.9 years	Sesame	No known reactions	6 mm	16.2	U, V, W	2 teaspoons tahini (~ 2 grams protein)
1.2 years	Soy	Never Ingested	5 mm	1.49	U, A	120 mL soymilk (~ 4 grams protein)
4.0 years	Walnut	Never Ingested	4 mm	4.05	S, OP, U	5 grams (~ 1.3 grams protein)
6.4 years	Wheat	Perioral rash	ND [†]	>100	OP, V, U	~ 1 gram protein
5.5 years	Wheat	Urticaria (but mother reported recent tolerance to accidental ingestion)	0 mm	10.3	U, C, W	1 slice bread (~ 4 grams protein)

SPT = skin prick test mean wheal diameter, sIgE = food-specific serum IgE level in kU_A/L, A = angioedema, U = urticaria, V = vomiting, C = cough, W = wheeze, D = dyspnea, S = sneeze, OP = oropharyngeal itching/pain,

* Reaction initially thought to be IgE-mediated but after challenge, history most-consistent with food protein induced enterocolitis syndrome given negative SPT and sIgE and nature of symptoms

[†] Patient unable to come off of anti-histamines for skin testing or for challenge